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# Abstracts

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**Immunopathological study of a 330 kilodalton (KD) brush border (BB) antigen. Role in Heymann's nephritis (HN).** *P. Ronco, J.T., Neale, C.B. Wilson, and P. Verroust. INSERM U64, Hopital Tenon, Paris, France, and Scripps Clinic and Research Foundation, La Jolla, California, USA.* Since gp 330 was identified by Kerjaschki and Farquhar, several groups have implicated in HN antigens of different molecular weight (150 to 600 kd). While analyzing with monoclonal antibodies (Mab) antigens expressed by BB and glomerulus, we identified a 330 kd protein localized in the coated pits of glomerular podocytes. We demonstrate here that this antigen is involved in HN. *(1)* The antigen is specifically bound by Ig eluted from glomeruli of rats with HN and by antibodies to the nephritogenic fraction RTE&5 purified by Edgington, Glassock, and Dixon in 1968. *(2)* Active immunization of Lewis rats with the antigen purified by affinity chromatography using S4B coupled Mab induces proteinuric membranous HN. *(3)* 5/6 Mab specific for the 330 kb antigen can induce passive HN. These results confirm the data of Kerjaschki and Farquhar and further indicate that the 330 kd antigen was a component of the purified antigen used by Edgington et al in 1968. In addition, they demonstrate that this antigen can by itself include clinically and histologically active HN, whereas the corresponding Mab can induce passive HN. These data confirm the role of in situ formation of Ig deposits in membranous glomerulonephritis.

**Immunohistochemical study of the C5b-9 complex of complement in diseased human kidneys: Diversity in localization and potential role in tissue damage.** *N. Hinglais, M.D. Kazatchkine, S. Bhakdi, Ch. Mandet, J. Grossetete, and J. Bariety.* The presence and localization of the C5b-9 neoantigens of the terminal complement sequence of C3c and C3d antigens and of Factor H antigens have been studied by immunofluorescence in 67 biopsy specimens from patients with a wide range of renal diseases with and without renal immune deposits. Seven biopsy specimens were also studied by electron microscopy using immunoperoxidase techniques. Biopsy specimens were classified into three groups based on the pattern of glomerular staining with anti-C5b-9. In the first group, a sparse mesangial labelling was seen, similar to that which had been observed in morphologically normal kidneys. In the second group, abundant clusters of C5b-9 were seen in enlarged mesangial areas. In group III, C5b-9 neoantigens were found in the same location as immune deposits. Immunoelectron microscopy demonstrated the presence of C5b-9 neoantigens on cell remnants embedded in connective matrices in all the specimens, the constant presence of C5b-9 neoantigens on old and large immune deposits, and the occasional presence of C5b-9 on recent and small immune deposits. The data indicated: *(1)* The presence of C5b-9 neoantigens even in large amounts, is not necessarily associated with immune deposits; *(2)* some immune deposits of small size do not activate the whole complement sequence, *(3)* the occurrence of proteinuria, in such cases, is independent of the presence or absence of C5b-9 on immune deposits (for example, membranous nephropathy, stage I), *(4)* in situ activation of the complement system may be documented in the absence of detectable C3 (C3c) antigen in glomeruli; and *(5)* morphological alterations of cells in the vicinity of immune deposits bearing C5b-9 are sparse and not constantly observed. Thus, the presence of C5b-9 neoantigens of the terminal complement sequence in pathological renal tissue does not have an univocal significance and requires appropriate controls in order to assess the potential role of C5b-9 in tissue damage in various types of immunologically mediated and non-immune human nephropathies.

**Successful treatment with cyclosporin of corticoresistant idiopathic nephrotic syndrome (minimal change lipoid nephrosis and focal segmental hyalinosis).** *A. Meyrier, P. Simon, G. Perret, and M.-C. Condamin-Meyrier. Hôpital Avicenne, Bobigny, and Hôpital La Bauchee, Saint-Brieuc, France.* The nephrotic syndrome (NS) of lipoid nephrosis (with minimal or no glomerular lesions, MCLN and of focal segmental hyalinosis (FSH) can be initially or secondarily resistant to corticosteroids and immunosuppressive agents. In such a case, the evolution of relentless NS is a hazardous and debilitating condition, which may eventually lead to end-stage renal failure. A functional disequilibrium between T and B lymphocytes and the role of a lymphokine that modifies glomerular permselectivity to proteins seem to play a pathogenetic role in these two conditions. In this respect, we reasoned that the mode of action of cyclosporin (CyA) could be compatible with a favorable effect on the NS. We therefore undertook treatment with CyA in four adults with corticoresistant NS. Renal function was normal or slightly subnormal in all. There were two women, 25 and 59 years of age, with MCLN and two men, 20 and 56 years of age, with FSH. The patients with MCLN had initially been corticosensitive, then corticodependent, and eventually corticoresistant. One case had received immunosuppressive treatment. The two individuals with FHS had been treated with corticosteroids, immunosuppressors, and, in one case, plasmapheresis, before they became resistant to any form of treatment. After a 28-day wash-out, ending in an 18-day placebo period, CyA was given for 3 months, at an initial dosage of 5 mg/kg/24 hr, which was subsequently adapted to keep whole blood levels in the range of 150 to 400 ng per liter. In one case of MCLN and in the two cases of FSH, partial remission was achieved (that is, NS subsided but low-grade proteinuria persisted), and, in one case of MCLN, complete remission was observed. The therapeutic effect of CyA was apparent between days 21 and 28. Renal and hepatic tolerance were good. In two of four cases, serum creatinine even decreased, probably due to amelioration of functional renal failure. This preliminary study shows that CyA is capable of inducing remarkable improvement in NS in which a therapeutic dead end has been reached. Several issues remain that concern: *(1)* the duration of the remission so obtained; *(2)* the advisable strategy in case of recurrence; and *(3)* the long term tolerance of CyA in such indications. Nonetheless, these observations show that CyA may represent a major advance in the management of NS resisting any other form of treatment. CyA could also be an immunologic tool of great interest in better understanding the nosology and the physiopathology of idiopathic NS.

**Hemoglobinuria in bare-handed drummers.** *A. Baumelou, E. Miailhe, B. Colin, and G. Berniot. Nephrology Department, Pitié Hospital, Paris, France.* The emission of dark urine, provoked by bare-handed drum beating, has been reported in only three case reports in the literature to our knowledge. This study stems from a case we observed. This work presents the results of history taking of 78 drummers and various functional studies completed on 11 of them. The frequency of this symptom was 61% in the population of drummers studied. It occurred primarily in male black professional drummers playing djembes or congas. The intensity and the length of drumming sessions are greater in this group. The finding of the sickle cell trait might constitute a factor for red blood cell (RBC) fragility in the black patients. Non-visible pigmenturia after performance is very frequent. Twenty-five post concert tests were performed on seven subjects using

Nephur-test urine dipsticks. We observed 17 positive reactions of the homogeneous type, reflecting the presence of free pigment rather than RBCs. Four subjects underwent complete upper and lower urinary tract investigation in the absence of detectable urine pigment. The results were normal, except for mild hypokalemia in three of them, corresponding most likely to urinary loss secondary to repeated cellular lysis. Two patients were studied before and after a drumming session: one patient presented obvious hemolysis after playing, with pinkish plasma, LDH 777 UI, haptoglobin 0.2 g/liter and hemoglobinuria with 10.6 g/liter, and proteinuria containing, in particular, an abundant amount of $\beta_2$ microglobin ($\beta_2$M). This abundant amount of $\beta_2$M in urine is likely linked to competitive tubular reabsorption of $\beta_2$M and hemoglobin. We conclude that hemolysis is a frequent phenomenon during lengthy bare-handed drumming sessions caused, no doubt, by repeated microtrauma to the fingertips and palms. This results in gross or non-visible hemoglobinuria and proteinuria. Their discovery after drumming sessions and later disappearance require no further urinary tract exploration.

**A new metabolic drug-induced nephrolithiasis: Oxalic stones in patients treated with piridoxilate.** *M. Daudon, R.J. Reveillaud, V. Kessali, M. Normand, and P. Jungers. Laboratoire Cristal, C.H. Saint-Cloud, Centre d'hémodialyse, Clinique de Toutes-Aures, Manosque, Polyclinique Saint-Martin, Pessac and Clinique Néphrologique, C.H.U. Necker, Paris, France.* Piridoxilate (P) is an equimolecular combination of glyoxylic acid and pyridoxine, the latter being added to prevent excessive production of oxalate from glyoxylate. The drug is used in the treatment of coronary disease and/or arteritis; the usual daily dose ranges from 110 to 165 mg of glyoxylate and 300 to 435 mg of pyridoxine. We observed seven patients, five male and two female, aged 43 to 80 years, who developed oxalic lithiasis after being treated with P for 9 months to 8 years. Six of them had no past history of urolithiasis. Stone formation clinically manifested 6 months to 5 years after starting P treatment. Four patients had bilateral, multiple, (10 to 70) and rapidly recurrent stones, whereas three had a single stone, and surgery was performed in six. Urine oxalate concentration, determined in only three patients, was 0.43 to 0.50 mmole/liter while on treatment, and decreased 0.13 to 0.23 mmole/liter after P withdrawal. The morphology of the stones of six patients was similar; it was of the whewellite type, but constantly with two peculiarities: *(1)* an irregular mammillary structure with a highly indented surface; and *(2)* on cross section, a powdered, unorganized nucleation area. Infrared spectroscopy (IR) revealed the typical spectrum of whewellite, both on the surface and the section, including the nucleation zone. Urinary sediment examination was performed in two patients while on treatment by P and revealed unusual crystalluria. Some crystals had an asymmetrical hexagonal shape; others were rectangular with convex extremities. I R analysis revealed oxalate trihydrate, a type of crystal usually not found in the urine. After P withdrawal, hexagonal and rectangular crystals disappeared. The seven patients have been followed for 3 to 30 months after P was stopped, and no recurrence of stones has been experienced by any of them. In conclusion, piridoxilate-induced urolithiasis appears to be more severe than most other drug-induced lithiasis reported to date. The disease is usually active, with production of rapidly recurrent stones, probably due to the high concentration of oxalic acid and presence of calcium oxalate crystals in urine. In patients on long-term treatment with P, a periodic search for urolithiasis is needed, and in stone formers such treatment should be avoided.

**Reversible acute renal failure (ARF) during enalapril treatment in a patient without renal artery stenosis (RAS).** *F. Brivet, D. Roulot, A. Poitrine, and J. Dormont. A. Beclere Hospital, Clamart, France.* ARF can occur during converting enzyme inhibition (CEI) for therapy for hypertension (HBP) due to single-kidney or bilateral RAS. We report ARF in a patient treated with CEI for HBP without RAS. The patient, a 62-year-old man was readmitted for HBP (260/150 mm Hg) despite clonidine, dihydralazine, amiloride, and hydrochlorothiazide treatment. Two years before, he was admitted for malignant varicella with ARF, encephalitis, hepatitis, pancreatitis, and HBP. Renal biopsy revealed focal glomerular sclerosis. At discharge, HBP was controlled; renal function was slightly impaired (creatinine 147 μmoles/liter). On readmission, despite increased therapy, HBP remained uncontrolled. Therefore, enalapril (10 mg/day) was initiated. Twenty hr later, ARF occurred (creatinine 400 μmoles/liter) without weight loss. ARF was reversible after enalapril withdrawal. No RAS was revealed by DIVA. To our knowledge, this is the first report of ARF during CEI treatment without RAS.

**Inefficiency of early prophylactic hemodialysis (HD) in cis-platinum (CDDP) overdose.** *F. Brivet, J.M. Pavlovitch, A. Gouyette, M.L. Cerrina, G. Tchernia, and J. Dormont. Hôpital A. Bleclere, Clamart, France.* CDDP may induce nephrotoxicity. HD was performed 4 hr after a CDDP overdose (200 mg/m²/8 hr), with the aim of limiting nephrotoxicity and myelosuppression. A 41-year-old nurse received on day 5 of the first course of polychemotherapy (stage III ovarian carcinoma) a double dose of CDDP. Day 1: doxorubicin (25 mg/m²), VM 26 (35 mg/m²); days 3 to 4: CPM (200 mg/m²), 5FU (350 mg/m²). At day 5, a 100 mg/m² CDDP perfusion was administered, inadvertently followed 6 hr later by a second dose (100 mg/m²). Nausea, diarrhea, headache, and metallic taste occurred 1 hr after second dose. Thus, 25% mannitol and 5% dextrose perfusions were started. HD was initiated in ICU 4 hr after the end of the second dose. Despite HD and osmotic polyuria, acute renal failure (ARF), metabolic acidosis, and febrile aplasia occurred 5 days after overdose. Patient (pt) was treated with 3 HD and nonspecific supportive therapy. Two weeks after CDDP perfusion, pt was discharged in good condition (creatinine 108 μmoles/liter). During the second course of chemotherapy (CDDP 50 mg/m²), ARF did not recur. HD ineffectiveness in preventing ARF is explained by lack of CDDP removal: 4.21 μg platinum/ml before HD versus 4.08 μg/ml after HD. CDDP plasma protein binding might be total 4 hr after perfusion. HD is not recommended in CDDP overdose; plasma exchange might be considered.

**Theophylline metabolites in the serum of uremic patients and in dialysis. Toxicity risks.** *G. Lachâtre, J.P. Charmes, P. Pignolet, M. Rincé, C. Leroux-Robert, and G. Nicot. Service de Pharmacologie Clinique, Service de Néphrologie, Hôpital Universitaire Dupuytren, Limoges, France.* Total body theophylline clearance in uremic patients is similar to that reported for patients with normal renal function. It is the same in subjects undergoing hemodialysis on the nondialysis day. Hemodialysis accelerates theophylline elimination. Nevertheless, we observe clinical toxic signs in dialysis patients with theophylline treatment and serum theophylline levels below 15 μg/ml. As several theophylline metabolites have been described, we used an HPLC method for determining serum concentrations of free and total theophylline and of its metabolites (1-methylxanthine, 3-methylxanthine, 1-methyluric acid, and 1,3-dimethyluric acid) in ten patients with normal renal function and in ten uremic patients, five in end-stage renal failure and five on maintenance hemodialysis. Other xanthine derivatives (1,7-dimethylxanthine, theobromine, and caffeine) were also evaluated in all these patients. Subjects with renal failure demonstrate theophylline values within or somewhat below the therapeutic range, with free fractions similar to those observed in healthy subjects. Moreover, the serum levels of theophylline metabolites observed in uremic patients are markedly increased. Since some of these metabolites have pharmacological and biochemical activities similar to those of their parent compound, we advise reconsidering the doses of theophylline usually given to patients with deteriorated renal function.

**An alternative means of blood access for chronic hemodialysis patients. The subcutaneous fixed superficial humeral artery.** *J. Zingraff, C. Naret, T. Drüeke, and M. Lacombe. Necker Hôpital, Paris, France.* Standard techniques of arteriovenous access to the circulation may be unsuitable in some hemodialysis patients because of the occurrence of hemodynamic complications or the exhaustion of all peripheral veins. We report on our experience in six hemodialysis patients in whom a subcutaneous fixed superficial humeral artery was used for long-term blood access. Mean age of the group was 55 years (range, 18 to 73). All these patients, four female and two male, were treated by hemodialysis during a mean period of 7 years (range, 1.5 to 18), and all had previous arteriovenous access devices accounting for the dilation of the humeral artery in the homolateral arm. The indication for the choice of a purely arterial access procedure was cardiac failure, at least partially due to an overfunctioning a-v fistula, in three patients, vascular steal syndrome in one patient, and exhaustion of all suitable venous sites in the two others. The period of observation ranged from 12 to 27 months (mean,

17). Arterial punctures were performed three times weekly during a mean period of 13.5 months (range, 0.5 to 26 months). No serious complications occurred. However, aneurysmal dilatation developed in two patients; in one, it was only of minor degree, but, in the other, the aneurysm was much larger. Only one hematoma was noteworthy in one patient. In conclusion, we propose the subcutaneous fixed superficial artery as an alternative means of blood access in some hemodialysis patients with precarious access problems and several failures of arteriovenous devices.

**A portable hemodialysis (HD) system with sorbent regeneration (SR) of dialysate (D).** *G. Mourad, R. Issautier, and C. Mion. Service de Néphrologie, Hôpital Lapeyronie, Montpellier, France.* To facilitate patient travel, we developed a simplified portable HD system utilizing the sorbent cartridge D3160 (O.T., Doxtel, Netherlands) for SR of D. There are three main components: *(1)* a compact disposable plastic container (DPC), 16 × 21 × 33 cm), used as D reservoir and surrounding the cartridge, assembled with a disposable PVC closed circuit for D recirculation; *(2)* a dialyser with A+V blood (B) lines; and *(3)* a roller pump receiving the pump segments of both B+D tubings, inducing similtaneously B+D flows in their respective circuits (mean ± SD, ml/min): QB 372 ± 30, QD 235 ± 19). D, prepared as recommended for SR, was kept at a constant temperature by external warming of DPC. Standard monitoring was used for B+D circuits. Simultaneous priming of D+B circuits permits quick and easy HD start. Our system was assessed in 20 patients during 26 4-hr HD sessions. D composition, checked every 30 min, showed an increase in D[Na] from 120 ± 13 (T0) to 152 ± 3 mmoles/liter (T240) with a stable pH (6.93 ± 0.24 to 6.71 ± 0.18). Extraction coefficients from B were: urea 0.58 ± 0.7; creatinine 0.50 ± 0.06; uric acid 0.67 ± 0.06; $PO_4$ 0.36 ± 0.14. B[Al] was 25.5 ± 12 before and 29 ± 14 μg/liter after HD. D[Al] (mean ± SD, μg/liter) remained below 10 (T0 7.42 ± 6.13; T60 4.1 ± 5.4; T120 4.1 ± 5.4; T180 4.6 ± 4; T240 8 ± 5.5) during HD sessions. HD tolerance was excellent despite an ultrafiltration rate of 2.55 ± 1.16 liters/session. Our system is an acceptable alternative to chronic HD system. Its compactness and portability permits greater patient freedom.

**Disappearance of mesangial IgA deposits in acute poststreptococcal glomerulonephritis superimposed on IgA nephropathy.** *P. Simon, M.P. Ramée, J.P. Grünfeld, D. Droz, G. Grateau, G. Cam, and K.S. Ang. C.H. Saint-Brieuc, C.H.U. Pontchaillou Rennes, Hôpital Necker, Paris, France.* Spontaneous disappearance of mesangial IgA deposits has never been documented in IgA glomerulopathy (GN). It has been rarely reported after renal transplantation or plasma exchanges. We report two cases in which disappearance of IgA deposits occurred concomitantly with acute poststreptococcal glomerulonephritis (AGN) superimposed on IgA GN. A 27-yr-old man with Berger's disease of 15 years' diagnosis and a 41-yr-old woman with IgA GN and alcoholic liver cirrhosis developed acute renal failure (peak serum creatinine 540 and 487 μmoles/liter, respectively with heavy proteinuria during streptococcal infection (rhinopharyngitis and surinfection of ascites fluid, respectively). In both patients (pts), serum antistreptolysins 0 were elevated and in one of them serum complement (CH50 and C3) decreased transiently. A second renal biopsy was performed in both pts. By light microscopy, there was diffuse endocapillary and mesangial glomerular proliferation with numerous neutrophls; humps were detected in one pt. These lesions had not been found on initial biopsy specimens. By immunofluorescence, IgA mesangial deposits had completely disappeared in one pt and were clearly attenuated in the other, whereas diffuse granular C3 deposits were observed along the GBM in both. Within a few weeks, renal function and proteinuria returned to basal levels: serum creatinine 210 and 150 μmoles/liters, proteinuria 5.2 and 2 g/24 hr, respectively. In conclusion, AGN may explain reversible renal failure in pts with IgA GN. Disappearance of IgA deposits may occur concomitantly, perhaps related to phagocytic activity of neutrophils that infiltrate glomeruli in AGN.